This is the accepted manuscript of the article, which has been published in **Scandinavian Journal of Surgery,** 2020.
http://dx.doi.org/10.1177/1457496919900411

Centralization of pancreatic surgery improves results. Review.

Journal:	*Scandinavian Journal of Surgery*
Manuscript ID	SJS-19-0263.R1
Manuscript Type:	Review article
Date Submitted by the Author:	21-Nov-2019
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Topics:	Hepato-pancreatic biliary surgery, Upper gastrointestinal surgery, Pancreas, Panreatic Neoplasm, Centralized Hospital Services, Carcinoma, Pancreatic Ductal
Abstract:	Background and aims. The effect of operation volume on the outcomes of pancreatic surgery has been a subject of research since the 1990s. In several countries around the world this has led to the centralization of pancreatic surgery. However, controversy persists as to the benefits of centralization and what the optimal operation volume for pancreatic surgery actually is. This review summarizes the data on the effect of centralization on mortality, complications, hospital facilities used and costs regarding pancreatic surgery. Materials and Methods. A systematic librarian-assisted search was performed in Pubmed covering the years from August 1999 to August 2019. All studies comparing results of open pancreatic resections from high and low-volume centres were included. In total 45 published articles were analysed. Results: Studies used a variety of different criteria for high-volume (HVC) and low-volume centres (LVC), which hampers the evaluating of the effect of operation volume. However, mortality in HVCs is consistently reported to be lower than in LVCs. In addition, failure to rescue critically ill patients is more common in LVCs. Cost-effectiveness has been also been evaluated in the literature. Length of hospital stay in particular has been reported be shorter in HVCs than in LVCs. Conclusion. The effect of centralization on the outcomes of pancreatic surgery has been under active research and the beneficial effect of it is associated especially with better short-term prognosis after surgery.

Centralization of pancreatic surgery improves results. Review

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Acknowledgements

We thank librarian Jaana Isojärvi for assisting the data search and Virginia Mattila for proofreading.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Declaration of conflicting interests

Authors have work experience in a high-volume centre.

Abstract

Background and aims. The effect of operation volume on the outcomes of pancreatic surgery has been a subject of research since the 1990s. In several countries around the world this has led to the centralization of pancreatic surgery. However, controversy persists as to the benefits of centralization and what the optimal operation volume for pancreatic surgery actually is. This review summarizes the data on the effect of centralization on mortality, complications, hospital facilities used and costs regarding pancreatic surgery.

Materials and Methods. A systematic librarian-assisted search was performed in Pubmed covering the years from August 1999 to August 2019. All studies comparing results of open pancreatic resections from high and low-volume centres were included. In total 44 published articles were analysed.

Results: Studies used a variety of different criteria for high-volume (HVC) and low-volume centres (LVC), which hampers the evaluating of the effect of operation volume. However, mortality in HVCs is consistently reported to be lower than in LVCs. In addition, failure to rescue critically ill patients is more common in LVCs. Cost-effectiveness has been also been evaluated in the literature. Length of hospital stay in particular has been reported be shorter in HVCs than in LVCs.

Conclusion. The effect of centralization on the outcomes of pancreatic surgery has been under active research and the beneficial effect of it is associated especially with better short-term prognosis after surgery.

Keywords: Pancreatic cancer; survival; pancreatic surgery; centralized hospital services

Introduction

The prognosis of pancreatic cancer is poor with an overall five-year survival rate of 5%. It is noteworthy that if the tumour is detected early, the prognosis improves and five-year survival as high as 30% can be achieved. Surgery coupled with oncologic therapy is the best option for patients in terms of survival. Pancreatic surgery is, however, high-risk surgery with over 40% postoperative morbidity rates and 0-15% postoperative mortality rates. In recent years, financial pressure has also reached health care organizers to search more cost-effective ways to take care of patients. The effect of the centralization on pancreatic surgery has been a subject of research worldwide since the 1990s. This review gathers published data on the effects of the centralization of pancreatic surgery on prognosis and cost-effectiveness.

Material and Methods

A systematic librarian assisted data search in Pubmed database was performed covering the time span from August 1999 to August 2019. Both Mesh terms and free text terms in pancreatic surgery, operation volume and centralization were used as search terms. The search yielded 141 articles which were manually evaluated. Studies comparing mortality, morbidity, complication distribution, pathologic reporting, long-term survival and/or costs in open pancreatic resections (PRs) (total pancreatectomy, pancreatoduodenectomy(PD) or distal resection(DP) or the combined results of these) between different volume groups were included. Studies not available in English were excluded, likewise those which did not involve pancreatic surgery or did not report results in relation to operation volume. No specific criterion was used in defining HVC or LVC. A PRISMA flowchart was drawn. The results of the studies were summarized in five categories: mortality, complications and failure to rescue, usage of hospital facilities, long-term survival and quality of pathology.

Results

Included studies

The systematic search yielded 141 studies. The search history is shown in Supplement 1. After exclusion, 44 studies were included, see flowchart in Figure 1. Eight studies were published on Scandinavia, 16 on other parts of Europe. In addition, the search found one study from Japan, Taiwan and Australia and ten 13 from North America. The search found four systematic reviews or meta-analyses of which four concentrated on the outcomes of surgery and one on methodological evaluation.

Definition of HVC

Several criteria have been proposed in the literature and no consensus has been reached. In studies from the Nordic countries (1-4) LVC has been defined as centre performing under 5-10 PDs annually except in one study (5) which analysed the data with a cutoff of 40 PDs. The definition of an HVC varied between 20 and 40 PDs per year in these same studies. Data on distal resections is sparse, but one study analysed their centralization with an HVC cutoff of 10 annual distal resections(6). Other European studies(7-19) have set the cutoff for an HVC at 15 to 77 PDs per year and for low-volume centre at under 16 PDs per year. Studies in the United States of America and Canada (20-28) have also presented a wide range for both HVCs and LVCs, from 3 to 22 PDs per year for LVCs and from 16 to 97 PDs per year for HVCs. A recent Japanese study (29) categorized hospitals with at least 18 PDs per year as HVCs and a maximum of 11 PDs per year as LVCs. Table 1.

Effect of operation volume on postoperative mortality

The effect of operation volume on mortality has been described is several studies: the data search found 33 studies reporting either mortality rates or hazard ratios for mortality in relation to hospital volume. Table 1. The reported a 30-day mortality rate or in-hospital mortality rate was 0-8.1% in HVCs and 3.5% - 15% in LVCs in the published studies. The 90-day mortality rate varied from 0% to 5.3% in HVCs and 9.3% to 16.1% in LVCs. Overall, studies report lower mortality rates in HVCs than in LVCs despite the heterogeneity of the volume criteria, but statistical significance was not reached in all studies on PRs, see Table 1. The mortality rates after PD (see Figure 2) resemble those for overall mortality after PR, probably due to high the proportions of PDs among the data of PRs. A recent meta-analysis by Hata et al. (30) pooled 13 studies and categorized studies according to different HVC criteria into three groups: HVC >19 PDs/year, HVC 20-29PDs/year and HVCs ≥30 PDs/year. Analysis of each group demonstrated a strong inverse association between operation volume and mortality. The pooled OR in HVC >19 PDs/year group was 1.94 (1.66-2.26), in HVC 20-29 PDs/year 2.34 (1.81-3.03) and HVCs ≥30 PDs/year 4.05 (1.96-8.34). Van Rijssen et al. (31) studied factors associated with postoperative mortality after PD among patients with suspicion of malignancy. They categorized hospitals not according to the operation volume but according to mortality. They found that male sex, age >75 years, BMI≥30, histopathological diagnosis of periampullary cancer and hospital volume were independent risk factors for failure to rescue.

A Swedish study by Derogar et al. (32) described the effect of teaching status and hospital volume on pancreatic surgery results in five operation volume categories. Most of their data comprised PDs (85%), but other pancreatic surgery was also included. They found only one significant difference: a decreased HR for 90-day mortality among hospitals performing four to six PRs per year when compared with a group performing a maximum of three PRs per year. They found a strong association between university hospitals and overall mortality favouring university hospitals (p=0.007). However, the data also included patients from the beginning of 1990, which may have affected the results.

Effect of operation volume on postoperative complications and failure to rescue

High operation volume was associated in several studies with fewer overall complications. Amini et al. (20) gathered data on PRs from the American NIS-database (Nationwide Inpatient Sample) covering some 20% of the community and teaching hospitals in USA. They stated that the OR for morbidity was 1.39-1.47 in low or medium volume centres compared with HVCs. Bateni et al. (21) (27,653 patients) and Mehta et al. (33) (2,453 patients) analysed the postoperative results of PRs and concluded that there were significantly more overall complications in LVCs than in HVCs. Mehta et al. (33) added that surgeon volume is also an independent risk factor for 30-day complication rate. A French nationwide study by El Amrani et al. (17) covering 12,333 patients reported that there was more septic, thromboembolic and haemorrhage complications in LVCs than in HVCs after pancreatic surgery. Ansari et al. (4) found the same in a Swedish study comprising 212 patients undergoing PD that haemorrhage complications especially are more common in LVCs than in HVCs and more blood transfusions are needed in LVCs. PDs were also analysed by Tran et al. (28) in a study of 15,599 patients. These authours added that cardiological, pulmonary and nephrologic disorders are more likely to occur in LVCs. Antila et al. (6) researched in a Finnish nationwide study distal resections and found that more delayed gastric emptying and gradus B/C pancreatic fistulas occur in LVCs than in HVCs.

Series by Ahola et al. (2) (466 PD patients) and Stella et al. (15) (108 PD patients) found no significant difference in the incidence of complications. However, Ahola et al. (2) demonstrated that fatal complications occur more often in LVCs than in HVCs. El Amrani et al. (17) agreed, stating that in addition to the higher incidence of septic and thromboembolic complications, more patients are lost in LVCs than in HVCs if these complications occur. The failure-to-rescue pattern has also been mentioned in American studies reporting results from the NIS database (11,081 PR patients) (34) and Medicare data (3,405 PR patients) (22). Gani et al. (34) reported that in HVCs (over 30 PRs/year) 5.4% of the cases presented a failure-to-rescue pattern vs. 11.1% in LVCs (under 8 PRs/year). Ghaferi et al. (22) added that the risk of failure-to-rescue is 3.12-fold in LVCs (max five PRs/year) vs. HVCs (> 27 PRs/year).

Effect of operation volume on long-term survival among pancreatic cancer patients

While the beneficial effect of centralization on short term prognosis has been shown in several studies, the role of operation volume on long-term survival among pancreatic cancer patients has been controversial. The data search resulted in eight studies describing the effect of operation volume on either median survival or survival rates among pancreatic cancer patients. Lidsky et al. (24) concentrated on PDs among 7,086 pancreatic cancer patients and Ahola et al. (1) reported survival after PRs among PDAC patients. Both studies resulted in significant differences in the median survival between LVCs and HVCs (16 months in LVCs vs. 20-26 months in HVCs). In addition, Gooiker et al. (9) added in their analysis of 11,160 PD patients that one and two-year survival is higher among patients operated on in HVCs than in LVCs (one-year survival 72% vs. 57% and two-year survival 40% vs. 31%). Risk for one-year mortality was also analysed by Alsfasser et al. (19) in a study covering 9,566 patients undergoing pancreatic surgery. They stated that OR is 1.73-1.3 in centres performing fewer than 77 PRs per year, but the data also included benign diseases, which challenges the interpretations of the results. Westgaard et al. (5) showed that five-year survival among PDAC patients undergoing PD may be higher in HVCs than in LVCs, 26% vs. 13%. However, Waterhouse et al. (35) with data on 270 and Derogar et al. (32) with data on 3,298 PRs found no association between hospital volume and long-term survival in their survival analyses. Waterhouse et al. (35) reported that patients operated on by surgeons performing fewer than four PRs per year had higher mortality rates and lower survival rates up to 1.5 years after surgery.

Effect of operation volume on pathology reports

The studies published on the quality of pathology demonstrated the beneficial cumulative effect of high operation volumes on pathological analyses. Four studies reported results on differences in pathological analyses or reporting. Onete et al. (36) reported that less information on tumour size or stage was found in the pathology reports in LVCs than in HVCs. This was corroborated by Ahola et al. (1) and Westgaard et al. (5), who added that tumour margin clearance evaluation was also more detailed in HVCs than in LVCs. These studies were based on data prior to 2010. A more recent study by Lidsky et al. (24) covering the years up to 2012 agreed with these authors the lower number of lymph nodes detected in LVCs than in HVCs. Standardization of pathology reporting has been shown to improve the quality of the analysis of PRs (37).

Use of hospital facilities

The effect of operation volume on the use of hospital facilities has been described in terms of length of hospital stay or stay in intensive care and reinterventions. Studies on PD patients (4) and distal resections (6) have presented that more re-operations are performed in LVCs than in HVCs. However, Ahola et al.(2) studying PD patients in a Finnish nationwide study and Stella et al. (15) concentrating on PRs found no significant difference between volume groups in frequency of reoperations among PD patients. A large study by Bateni et al. (21) comprising 27,653 patients undergoing PR revealed that re-admission is more common among patients operated on in LVCs than in HVCs. This was confirmed by Sutton et al. (26) in a survey of 9,805 PD patients. Length of hospital stay was also analysed in several studies resulting in the conclusion that hospital stay is shorter in HVCs than in LVCs (4,16,18,21,23-26,29,34,38). In addition, Ahola et al. (2) reported that hospital stay among Clavien-Dindo grade III patients was longer in LVCs than in HVCs. However, the Italian study by Stella et al. (15) found no significant difference between LVCs and HVCs in terms of hospital stay after a pancreatic resection. However, the comparison of studies is difficult without in-depth knowledge of the health system in each country.

Effect of operation volume on costs

The data search found nine retrospective studies and one meta-analysis on costs after pancreatic surgery. Ke et al. (39) published a systematic review of 19 studies on the effect of operation volume on costs in cancer surgery. The systematic review concluded that high operation volume leads to lower health care costs, but the evidence is inconsistent: 6/10 studies reported an inverse relationship between hospital volumes and costs, 3/10 a parallel relationship and one study no volume-related relationship. More recently, a retrospective study by Sutton et al. among PD patients (26) reported that high operation volume leads to significant cost savings among pancreatic cancer patients. The association was also apparent in several other studies reporting their results either on pancreatic cancer patients (29,38) (total of 14,691 patients) or all patients (2,28,40) (total of 16,387 patients). Enomoto et al. (13) added in an analysis of 3,137 patients from the NIS database that the costs for patients treated by low-volume surgeons at LVCs are higher than those for patients treated by low-volume surgeons at HVCs. On the other hand, large retrospective series by Gani et al. (34) (11,081 PR patients) (34) and Bateni et al. (21) (27,653 PR patients) found no significant association between costs and operation volume.

Cost-benefit has not been widely reported. Ahola et al. (2) analysed the cost-benefit association among pancreatic cancer patients by dividing costs by survival. The analysis showed that costs per survival are lowest among pancreatic cancer patients operated on at HVCs. Table 2.

Systematic reviews and meta-analyses

The search identified four systematic reviews or meta-analyses. Tol et al. (41) screened reviews published between 1980 and 2012. They analysed data in two categories: adjusted and non-adjusted data and discovered an inverse association between high operation volume and mortality. In addition, adjusted survival data also showed longer survival in HVCs. Hata et al. (30) studied articles published between 2001 and 2014 and analysed the volume effect on mortality, complications and hospital stay and agreed on a strong inverse association between mortality and hospital volume. Saulle et al. (42), concentrated on analysing hospital and surgeon volume. They reported that high surgeon volumes in HVCs result in beneficial outcomes, but that low surgeon volumes in HVCs also result in lower mortality, fewer complications and shorter hospital stay than in LVCs with low surgeon volumes. Halm et al. (43) performed a critical appraisal of the analysis of volume effect in 2002 and reported the problems of apparent variance in the study methods of different studies. The more recent meta-analysis mentioned above agreed that differences in the study settings limit the interpretations of the meta-analysis and, as shown in this review, still challenge the comparison of different studies.

Conclusion

The effect of hospital and surgeon volumes on the prognosis after a PR has been a subject of active research. The definition of HVC or LVC varies between studies, which complicates the comparison of different studies and no clear uniform criteria can be set. Despite the differences in the cutoffs, the published data highlights the beneficial effect of high operation volumes on mortality and failure-to–rescue. This may mirror the effect of cumulative knowledge, not only among surgeons, but among assisting specialities such as anaesthesiology, intensive care, interventional radiology and pathology in HVCs. It is noteworthy that many high-volume pancreatic surgery centres may also have high volumes in other fields of medicine and surgery. This may result in better availability of resources and personnel. These mechanisms speak for the centralization of high-risk surgery, such as pancreatic surgery.

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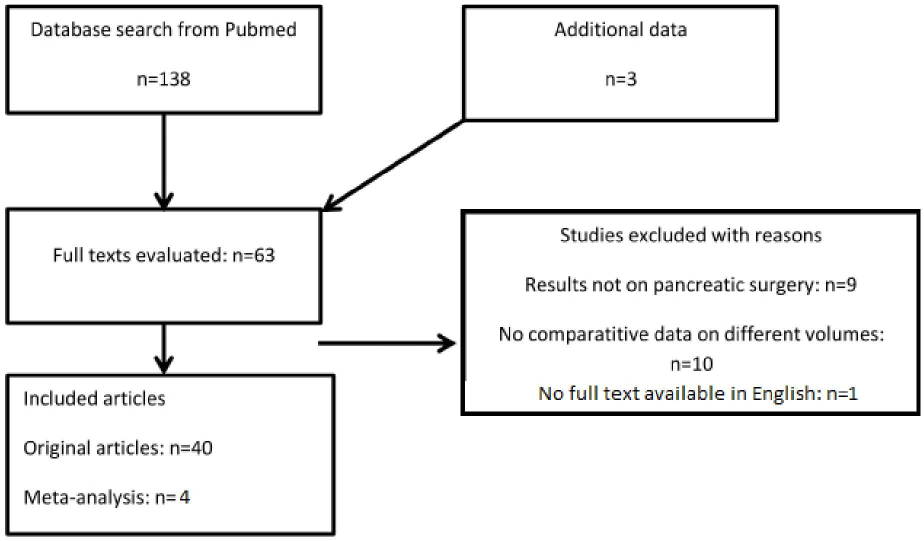

Flowchart of included studies.

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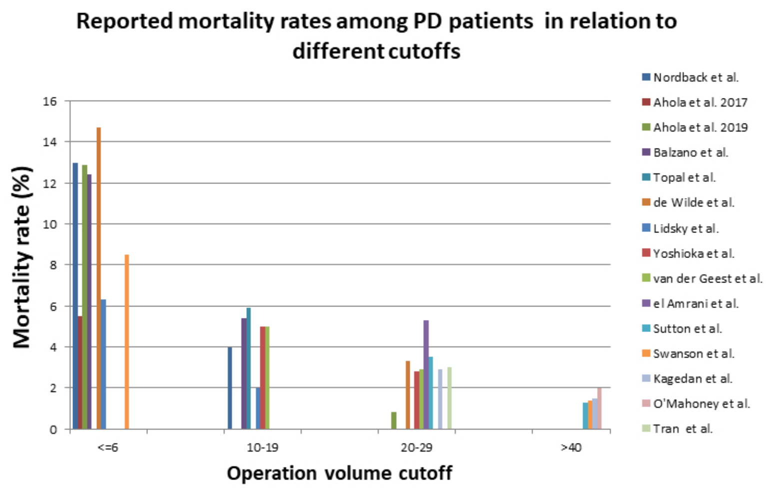

Reported mortality rates among PD patients.

81x60mm (300 x 300 DPI)

Search	Add to builder	Query	Items found	Time
#5	Add	Search **(#3) AND #4** Filters: **Publication date from 1999/08/01 to 2019/08/01; English**	138	07:35:43
#4	Add	Search **((centralized hospital services or hospitals, high volume or hospitals, low volume[MeSH Terms])) AND (centralization[Title/Abstract] OR centralisation[Title/Abstract] OR operation volume [Title/Abstract] OR hospital volume[Title/Abstract])** Filters: **Publication date from 1999/08/01 to 2019/08/01; English**	1098	07:33:15
#3	Add	Search **(#2) AND #1**	83869	07:18:11
#2	Add	Search **((surgical procedures, operative or pancreatectomy or pancreaticoduodenectomy or pancreaticojejunostomy[MeSH Terms])) OR (pancrea* surgery[Title/Abstract] OR pancreatoduodenectom*[Title/Abstract] OR pancreaticoduodenectom*[Title/Abstract] OR pancreaticojejunostom*[Title/Abstract] OR pancreatectom*[Title/Abstract])**	3029651	07:17:33
#1	Add	Search **((pancreatic neoplasm or pancreas[MeSH Terms])) OR (pancrea* neoplasm*[Title/Abstract] OR pancrea*[Title/Abstract] OR pancreatic adenocarcinom*[Title/Abstract])**	322686	07:15:12

Table 1.

	Total number of patients	**Definition of HVC/LVC**	**In-hospital mortality*/ 30-day mortality**		**90-day mortality**	
			HVC	**LVC**	**HVC**	**LVC**
Studies from the Nordic countries						
Nordback et al. 2002 (3) (Finland)	350	>10/<5 PDs	4%*	13%*		
Westgaard et al. 2009 (5) (Norway)	506	≥40/<40 PRs	_5.0%_	_7.5%_		
Ansari et al. 2014 (4) (Sweden)	221	≥25/<10 PDs	_0.0%*_	_4.0%*_		
Ahola et al. 2017 (1) (Finland)	467	≥20/<6 PDs	0%	5.5%	2.5%	11%
Ahola et al. 2019 (2) (Finland)	466	≥20/<6 PDs	0.8%	12.9%	1.9%	16.1%
Antila et al. 2019 (6) (Finland)	194	≥10/<4 DPs			_0%_	_0%_
Other European studies						
Balzano et al. 2008 (7) (Italy)	1,576	>14/≤ 6 PDs	5.9%	12.4%		
Topal et al. 2008 (18) (Belgium)	1,794	≥10/<10 PDs	5.4%*	10.7%*		
de Wilde et al. 2012 (8) (Netherlands)	2,155	>20/<5 PDs	3.3%*	14.7%*		
Gooiker et al. 2014 (9) (Netherlands)	11,160	≥20/≤9 PDs	_3.1%_	_5.2%_	_4.8%_	_7.4%_
Coupland et al. 2016 (10) (England)	2,580	≥30/<15 PRs	OR 0.78*	OR 1*		
Balzano et al. 2016 (12) (Italy)	10,936	33.5/5.5 PRs	5.0%*	8.9%*		
Alsfasser et al. 2016 (19) (Germany)	9,566	≥77/<12 PRs	OR=1*	OR=2.08 *	_OR=1_	_OR=1.99_

van der Geest et al.(11) 2016 (Netherlands)	3,420	≥40/<5 PDs			4.3%	9.7%
Farges et al. 2017 (13) (France)	22,366	>65/≤25 PRs			OR 1	OR 1.9
Stella et al. 2017 (15) (Italy)	108	≥50/≤5 PDs	*4.0%**	*7.0%**		
Krautz et al. (2018) (14) Germany	60,858	≥48/<16 PRs	8.1%*	10.4%*		
Capretti et al. 2018 (16) (Italy)	856	≥82/≤11 PRs	*2.4%*	*4.1%*		
el Amrani et al. 2018 (17) (France)	12,333	≥20/<10 PDs	5.3%*	9.1%		
Studies conducted elsewhere						
Ghaferi et al. 2011 (22) (USA)	37,865	27/≤2 PRs	3.1%*	13.3%*		
Sutton et al. 2014 (26) (USA)	3,411	≥97/≤22 PDs	1.3%*	3.5%*		
Swanson et al. 2014 (27) (USA)	21,482	≥40/<5 PDs	1.4%	8.5%	4.7%	14.2%
Yoshioka et al. 2014 (29) (Japan)	10,652	≥18/≤11 PDs	2.8%*	5%*		
Reames et al. 2014 (44) (USA)	30,732	≥17-41/≤2-5 PRs	3.2-4.2%	11-14%		
Amini et al. 2015 (20) (USA)	35,986	2000 – 2003: ≥29/<7.6 2004 – 2007: ≥50/<13, 2008 – 2011:≥99.5/<22 PRs.		OR=2.57 -2.14*		
Kagedan et al. 2016 (23) (Canada)	2,563	≥40/<20 PDs	1.5%	2.9%	2.7%	5.2%
O'Mahoney et al. (25) 2016 (USA)	17,761	≥61/<10 PDs	2.0%	9.3%		
Tran et al. 2016 (28)	15,599	≥20/<20 PDs	3%*	7.6%*		

(USA)						
Mehta et al. 2016 (33) (USA)	2,453	≥11/11 PRs	5.5%	13.9%		
Lidsky et al. 2017 (24) (USA)	7,086	≥16/≤3.3 PDs	2.0%	6.3%		
Gani et al. 2017, (34), (USA)	11,081	≤8/≥31 PRs	1.9%*	5.2%*		
Bateni et al.2018 (21) (USA)	27,653	≥19/<19 PRs	*1.2%**	*1.7%**		
HVC=high volume centre, LVC=low volume centre, OR=odds ratio, PD=pancreatoduodenectomy, DP=distal pancreatectomy, PR=pancreatic resection, *in-hospital mortality, *non-statistically significant difference in italics*						

Table 2

Study	Design	number of patients	Conclusion
Ke et al. 2012 (UK), (39)	meta-analysis		further studies are needed to evaluate the effect of centralization
Enomoto et al. 2013 (USA), (13)	retrospective data 2004-2008	3,317	shorter hospital stay in HVCs and lower costs
Yoshioka et al. 2013 (Japan), (29)	retrospective data 2007-2010	10,652	shorter hospital stay in HVCs and lower costs
Shi et al. 2014 (Taiwan), (38)	retrospective data 1998-2009	4,039	shorter hospital stay in HVCs and lower costs
Tran et al. 2015 (USA), (28)	retrospective data 2000-2010	15,599	lower costs in HVCs
Sutton et al. 2015 (USA), (26)	retrospective data 2009-2011	9,805	lower costs and fewer readmissions in HVCs
Williamsson et al. 2016 (Sweden), (40)	retrospective data 2005-2015	322	shorter hospital stay in HVCs and lower costs
Gani et al. 2017 (USA), (34)	retrospective data 2002-2011	11,081	no association between hospital volume and costs
Bateni et al. 2018 (USA), (21)	retrospective data 2013-2017	27,653	no association between hospital volume and costs
Ahola et al. 2019 (Finland), (2)	retrospective data 2012-2014	466	lower costs in HVCs